

foramen ovale 1, and bicuspid aortic valve 1. Additional surgical procedure was performed in each of the first 3 patients (4%). Postoperatively, IOTEE detected severe residual mitral regurgitation (MR) with marked systolic anterior motion (SAM) of the mitral valve in 3, ventricular septal defect in 1 patient, all of which (5%) were surgically corrected with a second pump run. All 3 cases of severe residual MR due to inadequate myectomy occurred during early surgical experience (1988 and 1989). Other 5 (7%) non-surgical postoperative findings included severe MR associated with poor LV function in 1, low ejection fraction in 2, hypovolemia with hypotension in 1 and regional wall motion abnormality in 1 patient. The mitral valve was structurally normal in 61 pts (82%), 3 (4%) had flail PMVL, 4 (5%) had PMVL prolapse, 1 had AMVL prolapse, 1 had bileaflet prolapse, 1 had valvular calcification and 4 had mitral annular calcification. SAM was present in 69 (93%) prebypass and was still present in 45 (61%) immediate postbypass and was present in 30 (41%) pre-discharge. The grade of MR decreased from  $2.3 \pm 1.0$  prebypass to  $1.1 \pm 0.5$  postbypass ( $p < 0.0001$ ). Absence of post-bypass SAM was associated with significant postoperative reduction of MR evaluated by IOTEE ( $p = 0.024$ ).

**Conclusion:** In patients with HOCM undergoing myectomy, IOTEE is valuable in detecting preoperatively unknown cardiac pathologies in 12%, altering surgical procedure in 4%, and in assessing the result of myectomy, requiring a second pump run in 5%. IOTEE was also valuable in identifying the etiology of postoperative LV dysfunction in 7% and intrinsic structural abnormality of mitral valve in 19%. Residual SAM detected by IOTEE after septal myectomy resolves in 33% of Pts by the time of predischARGE transthoracic echo study.

3:00

### 712-5 Dynamic Left Ventricular Outflow Tract Obstruction Immediately Following Aortic Valve Replacement: Detection by Intra-operative Trans-esophageal Echocardiography

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Aortic valve replacement (AVR) produces dramatic acute changes in left ventricular loading conditions that may provide a substrate for dynamic left ventricular outflow tract (LVOT) obstruction, particularly in the context of inotropic stimulation. This and related abnormalities have been described post-operatively, but their occurrence intra-operatively immediately post AVR has not been examined. To assess the prevalence and clinical impact of this phenomenon, intra-operative transesophageal echocardiography (TEE) was performed in 72 patients undergoing aortic valve replacement (AVR) for aortic stenosis ( $n = 28$ ) aortic regurgitation ( $n = 15$ ), or mixed aortic valve disease ( $n = 29$ ). There were 31 bioprostheses, 23 mechanical valves, and 18 homografts/autografts.

**Results:** No pt had dynamic LVOT obstruction on pre-bypass TEE. TEE performed after or during weaning from bypass revealed hemodynamically significant dynamic LVOT obstruction characterized by mitral systolic anterior motion, subvalvular obstruction and variable mitral regurgitation in 5 pts (2 homografts, 2 bioprostheses, 1 mechanical). All these pts had normal left ventricular function, concentric hypertrophy, and pre-op aortic stenosis  $\pm$  aortic insufficiency. Although all 5 pts were hemodynamically unstable (with difficulty weaning from bypass, variable systemic hypotension, and/or left atrial hypertension) dynamic LVOT obstruction was not suspected clinically prior to TEE. All pts improved with cessation of inotropes and/or  $\beta$ -blockade with coincident improvement, but not elimination of the subvalvular gradient.

**Conclusion:** Dynamic LVOT obstruction may occur following AVR in the immediate post-bypass period. This problem is difficult to recognize and may be inappropriately treated. Intra-operative TEE is essential to diagnose this problem and monitor therapy.

3:15

### 712-6 Detecting Myocardial Stunning During CABG Surgery with Myocardial Contrast Echocardiography (MCE)

Solomon Aronson, Anthony Fernandez, Christopher Young, Long Han, Alicia Toledano, Bryan Lee, Robert Karp, Stephen Feinstein, Robert Savage, Allan Klein, Bruce Lytel. *University of Chicago, Cleveland Clinic, Cleveland, Ohio*

During cardiac surgery, differentiating between ischemic and non-ischemic LV dysfunction is critical for prognosis and therapeutic strategies. We hypothesized that flow determined with myocardial contrast echo and wall motion analysis would enable identification of stunned myocardium. Twelve patients who received aortic root injections of Albunex<sup>R</sup> contrast during elective CABG surgery were compared to 14 matched controls for contrast agent safety. CPK enzymes, EKG, and hemodynamics were measured (pre- and post-op) for 72 hr. Baseline wall motion was scored (0-4) in contrast patients from 4 equally divided LV mid-papillary, short-axis regions and after CPB at the following intervals: 15, 30, 60 min.; 12 hr.; 5-8 days; and 30

days. Recorded images were analyzed off-line by 3 observers blinded to outcome. Contrast enhancement of myocardial perfusion at the time of surgery was also assessed in equally divided LV regions from the short-axis, LV echo image. Relationships between flow and function were described based on acute function (AF) (the avg. of scores at 15, 30, and 60 min after CPB), chronic function (CF) (the avg. of scores at 12 hr., 5 days, and 30 days), and intraoperative flow score.

**Results:** There were no significant differences pre- and post-op between control and contrast groups with respect to CPK enzymes, EKG changes, and hemodynamics. When coupled to function, flow was measured 60% of the time (29 of 48). Four relationships of flow and function were defined (function score of 0-2 = abnormal; 3-4 = normal):

Normal	AF = 3-4	flow normal	CF = 3-4
Stunned	AF = 0-2	flow normal	CF = 3-4
Hyperdynamic	AF = 3-4	flow abnormal	CF = 0-2
Other (post-op event)	AF = 3-4	flow normal	CF = 0-2

Relationship of Flow and Function by Region

Region	Normal	Stunned	Hyper	Other
Anterior 7	6	--	--	1
Posterior 9	6	3	--	--
Septal 7	5	--	2	--
Lateral 6	5	--	1	--
	76%	10%	10%	4%

**Conclusion:** Differentiation of non-ischemic and ischemic LV dysfunction appears possible with MCE and wall motion analysis. Myocardial stunning occurred 10% of the time after elective CABG surgery. Intraoperative flow and chronic function after CABG surgery are strongly linked (96%).

### 713 Basic Pharmacology

Monday, March 20, 1995, 2:00 p.m.-3:30 p.m.  
Ernest N. Morial Convention Center, Room 21

2:00

### 713-1 Inhibition of Neointimal Hyperplasia After Balloon Injury by Local Delivery of a Cyclic Arginine-Glycine-Aspartic Acid Peptide Targeting Vitronectin Receptor

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We have previously shown that cell-matrix interactions mediated via matrix protein ligand vitronectin (VN) derived from serum and its cell surface  $\alpha V\beta_3$  integrin receptor (VNR) regulate migration of human aortic smooth muscle cells (SMC) in vitro. Arginine-glycine-aspartic acid (RGD) sequence of VN (residues 45 to 47) is the critical domain for interactions. In this study we sought to determine whether interference with VN-VNR interaction in the arterial wall would alter development of neointimal hyperplasia in a rabbit model. After balloon-induced injury of the carotid artery (2 fr Fogarty, three times) serum-derived VN was observed in edematous intima and upper third of media (immunostaining,  $n = 3$ ). In 4 rabbits the VNR antagonist cyclic RGD peptide (1 mM) was locally applied to the injured artery by use of F-127 gel (800  $\mu$ l). RAD peptide (1 mM) served as an inactive control ( $n = 4$ ). At 28 days rabbits were killed and carotid arteries were fixed and mean intima and media area was determined by computer-assisted planimetry. The mean intima/media ratio in control balloon-injured arteries was  $0.47 \pm 0.04$  (SD). In injured, cyclic RGD peptide-treated arteries the intima/media ratio was  $0.11 \pm 0.02$  ( $p < 0.01$ ). There was no significant difference in media area in the two groups ( $1.84 \pm 0.22$  vs  $1.67 \pm 0.14$  mm<sup>2</sup>). These results suggest that 1) VN-VNR interaction mediates SMC migration in vivo, and 2) localized application of a VNR antagonist to the arterial wall after balloon injury modifies this process and results in a significant reduction in the development of neointimal hyperplasia. VN-VNR interaction may be an additional attractive target for pharmacologic manipulations aimed at limiting restenosis after vascular injury.

2:15

### 713-2 All Trans-retinoic Acid and Its Derivatives Inhibit Serotonin-Induced Vascular Smooth Muscle Cell Proliferation

Rajbabu Pakala, Peter J.A. Davies, Rosh Chandraratna, Claude R. Benedict. *University of Texas Medical School, Houston, TX; Allergan Inc., Irvine, CA*

**Background:** Serotonin (5HT), released from aggregating platelets at sites of vascular injury following coronary angioplasty, is a known mitogen for vascu-